

COVID-19 in 2021: Lessons Learned and Remaining Challenges

Anthony S. Fauci, M.D.
Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health



1

COVID-19 in 2021: Lessons Learned and Remaining Challenges

- Epidemiology
- Virology
- Transmission
- Diagnostics
- Clinical Course
- Therapeutics
- Vaccines

AS Fauci/NIH

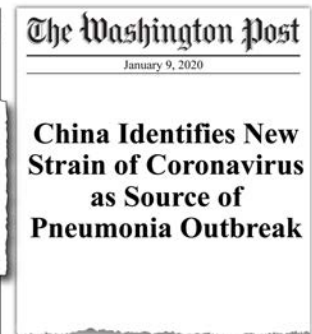
2

COVID-19 in 2021: Lessons Learned and Remaining Challenges

- Epidemiology
- Virology
- Transmission
- Diagnostics
- Clinical Course
- Therapeutics
- Vaccines

AS Fauci/NIH

3



AS Fauci/NIH

4

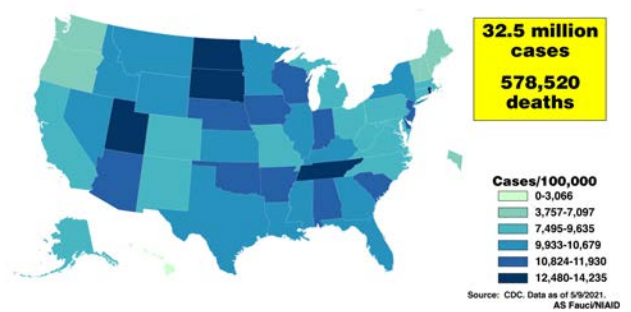
COVID-19 Globally



AS Fauci/NIH

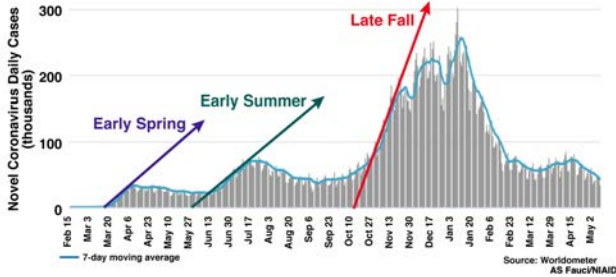
5

COVID-19 in the United States



6

Daily New COVID-19 Cases Reported in the United States - Slopes of 3 Surges



7



Viewpoint COVID-19 and Racial/Ethnic Disparities

MW Hooper, AM Nápoles and EJ Pérez-Stable

“The most pervasive disparities are observed among African American and Latino individuals, and where data exist, American Indian, Alaska Native, and Pacific Islander populations.”

AS Fauci/NIAD

8

COVID-19 in 2021: Lessons Learned and Remaining Challenges

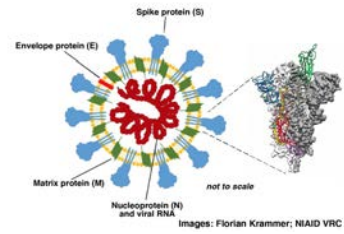
- Epidemiology
- Virology
- Transmission
- Diagnostics
- Clinical Course
- Therapeutics
- Vaccines

AS Fauci/NIAD

9

SARS-CoV-2 Virology

- **Beta-CoV:** same subgenus as SARS CoV-1 and some bat CoVs
- **RNA virus:** enveloped, positive-sense, single-stranded
- **Large genome:** ~30,000 Kb
- **4 structural proteins:** S, E, M, N
 - S allows virus to attach to and fuse with cell membrane
- **ACE2 receptor:** cell receptor



AS Fauci/NIAD

10

COVID-19 in 2021: Lessons Learned and Remaining Challenges

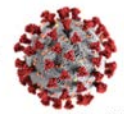
- Epidemiology
- Virology
- Transmission
- Diagnostics
- Clinical Course
- Therapeutics
- Vaccines

AS Fauci/NIAD

11

SARS-CoV-2 Transmission

- Mainly through exposure to respiratory droplets when close (≤ 6 ft) to an infected person
- Sometimes through droplets or particles that remain in the air (aerosols) over time and various distances ($>$ or < 6 ft)
- Less commonly through contact with contaminated surfaces
- Virus found in stool, blood, semen and ocular secretions; role in transmission unknown



AS Fauci/NIAD

12

Annals of Internal Medicine
 Established in 1927 by the American College of Physicians
 Published online January 22, 2021

The Proportion of SARS-CoV-2 Infections That Are Asymptomatic
 DP Oran and EJ Topol

- Available data suggest at least 1/3 of patients with SARS-CoV-2 infections never develop symptoms
- Longitudinal studies suggest ~3/4 of individuals with a positive PCR test who are asymptomatic at time of testing will remain asymptomatic

AS Fauci/NIID

13

JAMA Network | **Open**™ | January 7, 2021

SARS-CoV-2 Transmission From People Without COVID-19 Symptoms
 MA Johansson, JC Butler et al.

■ 59% of all SARS-CoV-2 infections result from asymptomatic transmission

- 35% from presymptomatic individuals
- 24% from individuals who never develop symptoms

AS Fauci/NIID

14

Fundamentals to Prevent Acquiring and Transmitting SARS-CoV-2

- Universal wearing of masks/cloth face coverings
- Maintain physical distance – at least 6 feet
- Avoid crowds and congregate settings
- Outdoors better than indoors
- Frequent washing of hands

AS Fauci/NIID

15

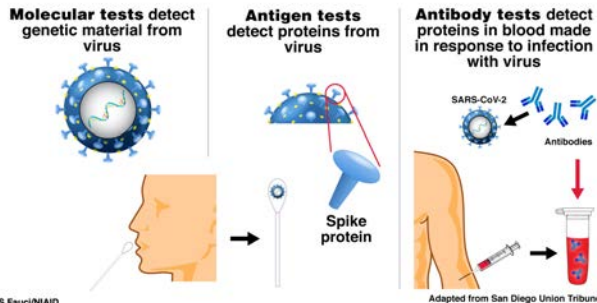
COVID-19 in 2021: Lessons Learned and Remaining Challenges

- Epidemiology
- Virology
- Transmission
- Diagnostics
- Clinical Course
- Therapeutics
- Vaccines

AS Fauci/NIID

16

Tests for SARS-CoV-2



AS Fauci/NIID

Adapted from San Diego Union Tribune

17

COVID-19 in 2021: Lessons Learned and Remaining Challenges

- Epidemiology
- Virology
- Transmission
- Diagnostics
- Clinical Course
- Therapeutics
- Vaccines

AS Fauci/NIID

18

COVID-19 Clinical Presentation

- Fever 83–99%
- Cough 59–82
- Fatigue 44–70
- Anorexia 40–84
- Shortness of breath 31–40
- Myalgias 11–35

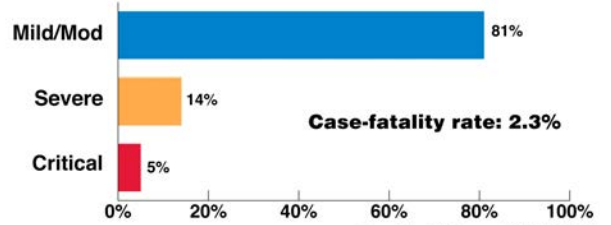
Other non-specific symptoms reported

- Sore throat, nasal congestion, headache, diarrhea, nausea, vomiting. Loss of smell/taste preceding the onset of respiratory symptoms.

Source: WHO, 5/2020 AS Fauci/NIID

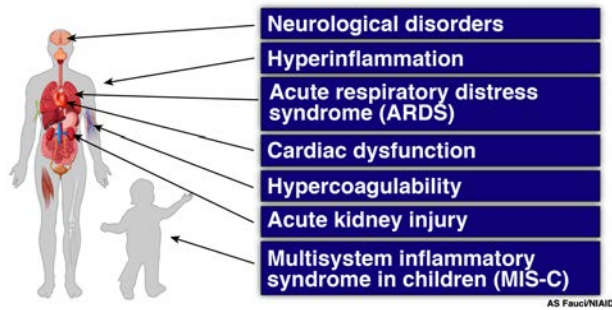
19

Spectrum of Disease Among 44,672 Individuals with Confirmed COVID-19, China



20

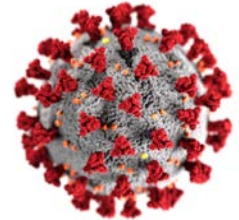
Manifestations of Severe COVID-19



21

People at Increased Risk for Severe COVID-19 Illness

- Older adults
- People of any age with certain underlying medical conditions



Source: CDC, 6/25/2020 AS Fauci/NIID

22

JAMA Network Open
February 19, 2021

Sequelae in Adults at 6 Months After COVID-19 Infection
JK Logue, HY Chu et al.

- Approximately 30% of patients enrolled at U. of Washington reported persistent symptoms for as long as 9 months after illness
- Fatigue most commonly reported symptom
- Persistent symptoms were reported by one-third of outpatients with mild disease

AS Fauci/NIID

23

COVID-19 in 2021: Lessons Learned and Remaining Challenges

- Epidemiology
- Virology
- Transmission
- Diagnostics
- Clinical Course
- Therapeutics
- Vaccines

AS Fauci/NIID

24

Selected Therapeutics for COVID-19

Therapeutics for early/moderate disease

- Remdesivir – FDA approved
- Monoclonal antibodies – EUA
 - Bamlanivimab; casirivimab+imdevimab;
 - bamlanivimab+etesevimab
- Convalescent plasma – EUA
- Other antivirals – clinical trials
- Hyperimmune globulin – clinical trials



Therapeutics for moderate/advanced disease

- Dexamethasone – standard of care
- Baricitinib+remdesivir – EUA
- Immunomodulators (e.g. tocilizumab) – clinical trials
- Anticoagulants – clinical trials

AS Fauci/NIAD

25

NIH National Institutes of Health
Turning Discovery Into Health
Tuesday, April 21, 2020

News Release

Expert U.S. Panel Develops NIH Treatment Guidelines for COVID-19

“Living document” updated often as new clinical data accrue

[Covid19treatmentguidelines.nih.gov](https://www.covid19treatmentguidelines.nih.gov)

AS Fauci/NIAD

26

Identification of Vulnerable Targets in the SARS-CoV-2 Replication Cycle

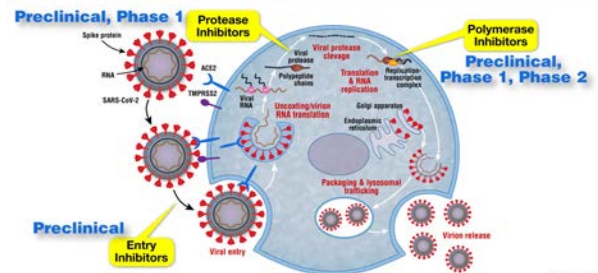


Design Drugs to Inhibit Vulnerable Targets

AS Fauci/NIAD

27

SARS-CoV-2 Replication Cycle: Targets for Antiviral Therapeutics



AS Fauci/NIAD

28

COVID-19 in 2021: Lessons Learned and Remaining Challenges

- Epidemiology
- Virology
- Transmission
- Diagnostics
- Clinical Course
- Therapeutics
- Vaccines

AS Fauci/NIAD

29

April 9, 2021
Vol. 372, Issue 6338

Science

The Story Behind COVID-19 Vaccines

Anthony S. Fauci

“The speed and efficiency with which these highly efficacious vaccines were developed and their potential for saving millions of lives are due to an extraordinary multidisciplinary effort involving basic, preclinical, and clinical science that had been under way—out of the spotlight—for decades before the unfolding of the COVID-19 pandemic.”

AS Fauci/NIAD

30

Selected COVID-19 Vaccines

Platform	Developer	Status
Nucleic Acid (mRNA)	moderna	■ EUA
	BIONTECH	■ EUA
Adenovirus Vector	Johnson & Johnson	■ EUA
	AstraZeneca	■ EUA TBD
Recombinant Protein and Adjuvant	gsk SANOFI	■ Phase 2 clinical trial launched Feb. 2021
	NOVAVAX	■ EUA TBD

AS Fauci/NIID

31

COVID-19 Vaccines are:

- Efficacious in clinical trials
- Effective in real-world settings
- Safe

AS Fauci/NIID

32

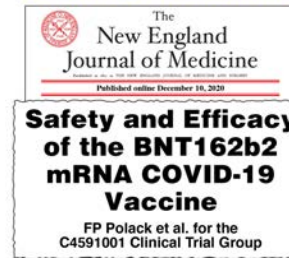
COVID-19 Vaccines are:

- Efficacious in clinical trials
- Effective in real-world settings
- Safe

AS Fauci/NIID

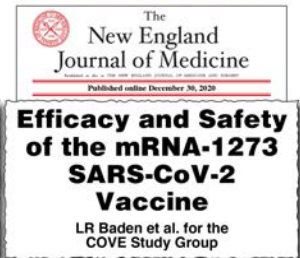
33

Pfizer/BioNTech Vaccine



■ Efficacy: 95%

Moderna Vaccine



■ Efficacy: 94.1%

AS Fauci/NIID

34

Johnson & Johnson (Janssen) Vaccine



Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine against COVID-19
J Sadoff et al. for the ENSEMBLE Study Group

- 66% efficacy overall vs. moderate-to-severe COVID-19
 - 72% in United States
 - 68% in Brazil
 - 64% in South Africa
- 85% efficacy vs. severe disease across all regions studied

AS Fauci/NIID

35

COVID-19 Vaccines are:

- Efficacious in clinical trials
- Effective in real-world settings
- Safe

AS Fauci/NIID

36

“Real World” Vaccine Effectiveness Studies

The New England Journal of Medicine
 Published online March 23, 2021

Early Evidence of the Effect of SARS-CoV-2 Vaccine at One Medical Center
 W Daniel, DK Podolsky et al.

- 23,234 employees of University of Texas Southwestern Medical Center, Dallas, TX; vaccination program initiated 12/15/2020
- 0.05% infection rate among fully vaccinated employees

CDC Centers for Disease Control and Prevention
 CDC 247: Saving Lives. Protecting People™ April 2, 2021
 Morbidity and Mortality Weekly Report (MMWR) Volume 70, Number 13

Interim Estimates of Vaccine Effectiveness of BNT162b2 and mRNA-1273 COVID-19 Vaccines in Preventing SARS-CoV-2 Infection Among Health Care Personnel, First Responders, and Other Essential and Frontline Workers — Eight U.S. Locations, December 2020–March 2021

- Prospective study; n=3,950
- mRNA vaccine effectiveness of full immunization (≥14 days after second dose) was 90% against SARS-CoV-2 infections regardless of symptom status; 80% after one dose
- 3 PCR-confirmed infections occurred during 78,902 person-days with full immunization (0.04/1,000 person-days)

AS Fauci/NIID

37

THE LANCET

published online May 5, 2021

Impact and Effectiveness of mRNA BNT162b2 Vaccine Against SARS-CoV-2 Infections and COVID-19 Cases, Hospitalisations, and Deaths Following a Nationwide Vaccination Campaign in Israel: An Observational Study Using National Surveillance Data

EJ Haas, S Alroy-Preis et al.

AS Fauci/NIID

38

Estimated Effectiveness of 2 Doses of Pfizer/BioNTech COVID-19 Vaccine Against 6 Outcomes, Israel

- All ages, 201.9 million person-years total
- B.1.1.7 variant accounted for ~95% of SARS-CoV-2 infections

Estimated adjusted effectiveness, ≥7 days after the second dose, Jan 24 to April 3, 2021

SARS-CoV-2 infection	95.3%
Asymptomatic SARS-CoV-2 infection	91.5
Symptomatic COVID-19	97.0
COVID-19-related hospitalization	97.2
Severe or critical COVID-19-related hospitalization	97.5
COVID-19-related death	96.7

AS Fauci/NIID

Source: EJ Haas et al. Lancet, 5/5/2021.

39

Estimated Effectiveness of 2 Doses of Pfizer/BioNTech COVID-19 Vaccine Against SARS-CoV-2 Infection, by Age Group, Israel

Estimated adjusted effectiveness, ≥7 days after the second dose, Jan 24 to April 3, 2021

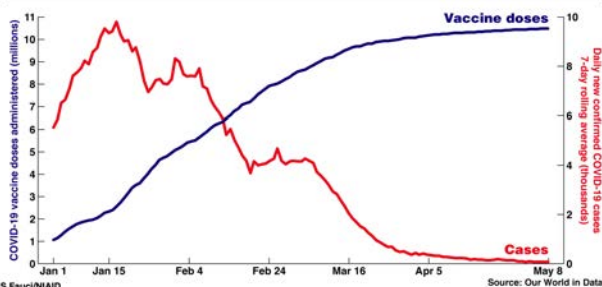
Age Group	VE vs. SARS-CoV-2 infection
All ages	95.3%
Age 16-44 years	96.1
Age 45-64 years	94.9
Age ≥65 years	94.8
Age ≥75 years	95.1
Age ≥85 years	94.1

AS Fauci/NIID

Source: EJ Haas et al. Lancet, 5/5/2021.

40

Effect of Robust COVID-19 Vaccination Effort in Israel, Where B.1.1.7 Predominates



AS Fauci/NIID

Source: Our World in Data

41

Impact of Viral Variants on Vaccine Effectiveness

AS Fauci/NIID

42

Wild Card: SARS-CoV-2 Variants

B.1.1.7 originally United Kingdom	<ul style="list-style-type: none"> Covered well by currently authorized mRNA vaccines; likely covered by J&J vaccine but more data needed
B.1.351 originally South Africa	<ul style="list-style-type: none"> Moderately to severely reduced vaccine efficacy for some vaccines -- J&J 64% efficacy vs. moderate/severe/critical disease; Novavax 43% efficacy vs. symptomatic disease; AstraZeneca 10% efficacy vs. symptomatic disease; Pfizer/BioNTech 100% efficacy vs. symptomatic disease (small numbers in clinical trial); 75% effectiveness (Qatar)
P.1 originally Brazil	<ul style="list-style-type: none"> Vaccine efficacy unknown (no clinical trials) In vitro -- minimal/moderate loss of neutralizing activity by vaccine-induced antibodies
B.1.429/B.1.427 originally California	<ul style="list-style-type: none"> Vaccines are likely still effective In vitro -- moderate loss of neutralizing activity by vaccine-induced antibodies
B.1.526 originally New York	<ul style="list-style-type: none"> Vaccine efficacy unknown In vitro -- variable loss of neutralizing activity by vaccine-induced antibodies
B.1.617 originally India	<ul style="list-style-type: none"> Vaccine efficacy unknown In vitro -- very limited data

AS Fauci/NAID

43



Effectiveness of the BNT162b2 COVID-19 Vaccine against the B.1.1.7 and B.1.351 Variants

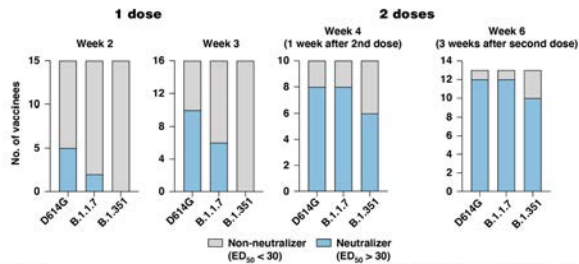
LJ Abu-Raddad et al. for the National Study Group for COVID-19 Vaccination

- Mass vaccination campaign in Qatar; total n=385,853
- Vaccine effectiveness against any documented infection
 - B.1.1.7 -- 89.5% after 2 doses, 29.5% after 1 dose
 - B.1.351 -- 75.0% after 2 doses, 16.9% after 1 dose
- Vaccine effectiveness against severe, critical, or fatal disease
 - B.1.1.7 -- 100% after 2 doses, 54.1% after 1 dose
 - B.1.351 -- 100% after 2 doses, 0% after 1 dose

AS Fauci/NAID

44

Improved Neutralization of SARS-CoV-2 Variants After 2nd Pfizer Vaccine Dose



AS Fauci/NAID

Source: D Planas et al. Nature Med, March 26, 2021.

45

COVID-19 Vaccines are:

- Efficacious in clinical trials
- Effective in real-world settings
- Safe

AS Fauci/NAID

46

Ensuring COVID-19 Vaccine Safety in the U.S.

- Clinical trials
- Expanded safety monitoring systems
 - CDC: V-safe
 - CDC: National Healthcare Safety Network (NHSN)
 - FDA: Other large insurer/payer databases
- Other safety monitoring systems
 - CDC and FDA: Vaccine Adverse Event Reporting System (VAERS)
 - CDC: Vaccine Safety Datalink (VSD)
 - CDC: Clinical Immunization Safety Assessment (CISA) Project
 - FDA and the Centers for Medicare and Medicaid Services: Medicare data
 - FDA: Biologics Effectiveness and Safety System (BEST)
 - FDA: Sentinel Initiative
 - DoD, VA systems

AS Fauci/NAID

Source: <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/reporting-systems.html>

47

70% of adults vaccinated with at least 1 dose by July 4

AS Fauci/NAID

48

The Race is On



AS Fauci/NIH